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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/524,747	03/14/2000	Alberto Reiner	622-39	8132

7590 02/12/2004

Leonard C Mitchard
Nixon & Vanderhye PC
1100 North Glebe Road 8th Floor
Arlington, VA 22201

EXAMINER	
OWENS JR, HOWARD V	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/524,747	REINER ET AL.	
	Examiner	Art Unit	
	Howard V Owens	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/3/2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/3/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/3/2003 has been entered.

35 U.S.C. 102 rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20 – 29 are under 35 U.S.C. 102(b) as being anticipated by Granger, EP 466650 for the reasons of record set forth below.

Claims 20 -29 are drawn to a method for obtaining an average Cmax of Diclofenac via administration of diclofenac in acid and/or salt form together with sodium/potassium bicarbonates in which the alkali metal bicarbonates are present in an amount of from 20 to 80% by weight of diclofenac.

Granger anticipates the claims as it teaches a pharmaceutical formulation comprising a non-steroidal anti-inflammatory and a metal base or basic salt such as hydroxide, sulfate, carbonate, bicarbonate, subcarbonate, or trisilicate; wherein the nonsteroidal anti-inflammatory may be diclofenac and the alkali metal can be aluminum, sodium, magnesium, potassium or bismuth (pp. 1 and 2). Granger further discloses that

the metal base or basic salt may be administered in an amount ranging from about 25 to about 100% (p.2, line 57 - p.3, line 5).

Granger also teaches that the pharmaceutical formulation or composition comprising the non-steroidal anti-inflammatory agent such as dicoflenac may be administered in admixture with suitable pharmaceutical diluents, excipients or carriers and that the active drug components may be combined with any oral nontoxic pharmaceutically acceptable inert carrier such as lactose, starch, sucrose, etc. Furthermore, that sweetening and flavoring agents and preservatives can also be included where appropriate (p. 3, lines 6-23) anticipating the presence and amount of at least one flavoring substance, be it mint, aniseed and ammonium glycyrrhizinate as these flavoring substances could be adjusted in proportion to suit an appropriate taste. Granger also teaches the use of disintegrating agents such as methylcellulose and cross-linked PVP (p.3, lines 16-23) which anticipate the use of immediate and delayed release layers.

Granger discloses that the metal base or basic salt is co-administered with fenamic acid derivatives or non-steroidal systemic anti-inflammatory agents to confer a cytoprotective effect or reduce the gastrointestinal inflammation associated with administration of these agents (p.2, lines 20-58).

Although Granger does not explicitly teach the T_{max} and C_{max} values, the T_{max} and C_{max} values are a function of administering the diclofenac with the metal base or basic salt wherein the concentration of the metal base or basic salt is 20-80% by weight; thus, given that Granger teaches administration of diclofenac or fenamic acid derivatives with a metal base or basic salt wherein the concentration of the basic salt is analogous to that of applicant, 25%-100%, the T_{max} and C_{max} values would be inherently achieved.

Applicant's chief argument is that the teachings of Granger do not anticipate applicant's discovery of the T_{max} and C_{max} values because the dissolution profile for that of the bicarbonate form is significantly greater than that of the 4 other metal basic salt forms taught by Granger. Applicant has submitted a declaration to purportedly support the unexpected advantage of the invention.The declaration filed under 37 CFR 1.132 filed

9/16/02 is insufficient to overcome the rejection of claims 13,14,16-23 and 25-28 based upon Granger, EP 0466650 as set forth in the last Office action.

The Reiner declaration attempts to show that even though one of skill in the art would recognize that Granger teaches a diclofenac composition with sodium or potassium bicarbonate, one of skill in the art could not expect the dissolution profile of sodium/potassium bicarbonate to be exemplary of all the metal basic salts disclosed by Granger since there are 5 additional basic salts and 3 additional metals disclosed. However, applicant only compares two other metal basic salts with sodium bicarbonate, magnesium/calcium carbonate and aluminum hydroxide. The data presented on p. 3 of the declaration actually shows that the carbonate dissolution profile is comparable to the bicarbonate form. The aluminum hydroxide form has a lower dissolution profile, however, this does not overcome the fact that Granger teaches the use of sodium bicarbonate as one of the more effective metal basic salt to be used with a non-steroidal anti-inflammatory. Granger teaches in Example 2 that sodium bicarbonate demonstrated the greatest change in the reduction of ulcer formation when co-administered with a non-steroidal anti-inflammatory. Thus the prior art has established the motivation for using the sodium bicarbonate form with a non-steroidal anti-inflammatory such as the fenamic acid derivative of diclofenac.

The Marzo declaration under 37 CFR 1.132 filed 11/3/2003 is insufficient to overcome the rejection of claims 20 - 29 based upon Granger, EP 466650 as set forth in the last Office action because: The evidence is comparable to Reiner in that it attempts to distinguish the invention from that of the prior art by the demonstration of various dissolution profiles that are not contemplated in the prior art. An explanation of dissolution profiles is not probative to the question of whether the prior art recognizes the combination of diclofenac with the claimed alkali metal salts at the claimed concentration. Moreover, the declaration is primarily based on the assertion that Granger does not disclose the claimed formulation because there are no working examples. A reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F. 2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966). As

cited supra, Granger anticipates the claims as it teaches a pharmaceutical formulation comprising a non-steroidal anti-inflammatory and a metal base or basic salt such as hydroxide, sulfate, carbonate, bicarbonate, subcarbonate, or trisilicate; wherein the nonsteroidal anti-inflammatory may be diclofenac and the alkali metal can be aluminum, sodium, magnesium, potassium or bismuth (pp. 1 and 2). Granger further discloses that the metal base or basic salt may be administered in an amount ranging from about 25 to about 100% (p.2, line 57 - p.3, line 5).

If the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, the disclosure should be regarded as sufficient. Failure to appreciate a result is of no import if the result is a necessary consequence of what was deliberately intended, *Mehl/Biophile Int. Corp. v. Milgraum*, U.S. C.A.F.C., 52 USPQ2d 1303 . The invention is still oral administration of diclofenac with an alkali metal bicarbonate, the preamble language asserting a dissolution value is not given patentable weight. Since Granger not only teaches the co-administration of sodium bicarbonate with a fenamic acid derivative in the claimed concentration range and demonstrates that the sodium bicarbonate form is one of the more effective basic salt forms of those disclosed to be co-administered with a fenamic acid derivative, applicant's discovery that there is a dissolution profile associated with administering diclofenac with the same metal basic salt in the same concentration is seen as the recognition of an inherent effect associated with that administration.

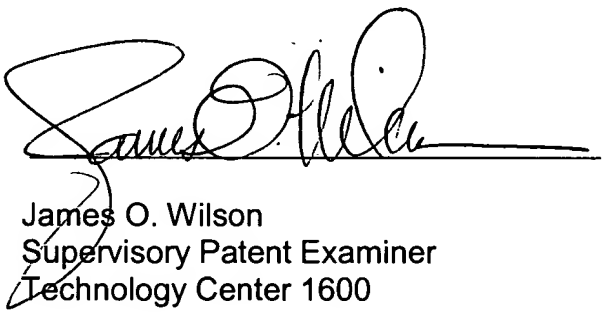
For the reasons set forth above, the 35 U.S.C. 102 (b) rejection is maintained.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE**

FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Howard V. Owens
Patent Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.